

U.S.S.N 10/071,016  
GRUENBERG  
PRELIMINARY AMENDMENT

A<sup>1</sup>  
*Biology 55:437*) and reduces the proliferation and IFN- $\gamma$  production (a Th1 cytokine) of peripheral blood T-cells and T-cell clones (Taga *et al.* (1993) *Journal of Immunology* 150:4754; de Waal Malefyt *et al.* (1993) *Journal of Immunology* 150:4754). RCC supernatants increase the production of IL-10 from macrophages (Ménétrier-Caux *et al.* (1999) *British Journal of Cancer* 79:119). The Th2 cytokines, IL-10 and IL-4, are also produced by RCC TIL (Schoof *et al.* (1993) *Cellular Immunology* 150:114; Wang *et al.* (1995) *International Journal of Cancer* 61:780; Maeurer *et al.* (1995) *Cancer Immunology, Immunotherapy* 41:111). IL-10 serum levels are increased in sera of subjects with solid tumors and correlates with poor responsiveness and decreased survival (De Vita *et al.* (2000) *Oncology Reports* 7:357). Increased serum concentrations of IL-10 can be a predictor of unfavorable outcome in RCC (Elsässer-Beile *et al.* (1999) *Cancer Immunology, Immunotherapy* 48:204). RCC cells also produce other immunosuppressive cytokines, such as IL-6, IL-8 and TGF- $\beta$ .

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**IN THE CLAIMS:**

Please replace claim 47 with the following;

A<sup>2</sup>  
47. (Amended) A process for producing compositions that have an enhanced population of activated polyclonal Th1 memory cells, comprising:  
(a) collecting a sample of mononuclear cells from a subject;  
(b) expanding and differentiating the mononuclear cells by repeatedly activating T-cells in the mononuclear cell sample in the absence of exogenous growth or differentiation factors, thereby producing a highly pure population of activated polyclonal Th1 memory cells.

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**REMARKS**

Any fees that may be due in connection with filing this paper, or with this application during its entire pendency, may be charged to Deposit Account No. 50-1213.

The specification and the claims are amended to correct obvious typographical, spelling, and grammatical errors.

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No new matter has been added.

Entry of this amendment is respectfully requested.

\* \* \*

Respectfully submitted,  
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By: \_\_\_\_\_

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Applicant: Micheal L. Gruenberg

Serial No.: 10/071,016

Filed: February 7, 2002

For: Th1-CELL ADOPTIVE  
IMMUNOTHERAPY

Art Unit: 1636

Examiner: Unassigned

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Date of Deposit August 15, 2002

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TECH CENTER 1600/2900ATTACHMENT TO THE PRELIMINARY AMENDMENT  
MARKED UP PARAGRAPHS AND CLAIMS (37 CFR §1.121)

## IN THE SPECIFICATION:

Please amend the paragraph on page 22, lines 3-28, as follows:

Tumor cells are known to produce a variety of Th2 cytokines (Chen *et al.* (1994) *International Journal of Cancer* 56:755; Asselin-Paturel *et al.* (1998) *Journal of Cancer* 77:7; Smith *et al.* (1994) *American Journal of Pathology* 145:18; Vowels *et al.* (1994) *Journal of Investigative Dermatology* 103:669; Nitta *et al.* (1994) *Brain Research* 649:122). Tumor infiltrating cells also produce Th2 cytokines (Roussel *et al.* (1996) *Clinical and Experimental Immunology* 105:344). Freshly isolated RCC cells produce IL-10 (Nakagomi *et al.* (1995) *International Journal of Cancer* 63:366; Wang *et al.* (1995) *International Journal of Cancer* 61:780), a Th2 cytokine. IL-10 is a potent inhibitor of tumor cytotoxicity (Nabioullin *et al.* (1994) *Journal of Leukocyte Biology* 55:437) and reduces the proliferation and IFN- $\gamma$  production (a Th1 cytokine) of peripheral blood T-cells and T-cell clones (Taga *et al.* (1993) *Journal of Immunology* 150:4754; de Waal Malefyt *et al.* (1993) *Journal of Immunology* 150:4754). RCC supernatants increase the production of IL-10 from macrophages (Ménétrier-Caux *et al.* (1999) *British Journal of Cancer* 79:119). The Th2 cytokines, IL-10 and IL-4, are also produced by RCC TIL (Schoof *et al.* (1993) *Cellular Immunology* 150:114; Wang *et al.* (1995) *International Journal*

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*of Cancer 61:780; Maeußer et al. (1995) Cancer Immunology, Immunotherapy 41:111). IL-10 serum levels are increased in sera of subjects with solid tumors and correlates with poor responsiveness and decreased survival (De Vita et al. (2000) Oncology Reports 7:357). Increased serum concentrations of IL-10 can be a predictor of unfavorable outcome in RCC (Elsässer-Beile et al. (1999) Cancer Immunology, Immunotherapy 48:204). RCC cells also produce other immunosuppressive cytokines, such as IL-6, IL-8 and TGF- $\beta$ .*

**IN THE CLAIMS:**

**Please amend claim 47 as follows;**

47. (Amended) A process for producing compositions that have an enhanced population of activated polyclonal Th1 memory cells, comprising:

(a) collecting a sample of mononuclear cells from a subject;

(b) expanding and differentiating the mononuclear cells by repeatedly activating T-cells in the mononuclear cell sample in the absence of exogenous growth or differentiation factors, thereby producing a highly pure population of activated polyclonal Th1 memory cells.

\* \* \*

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